

CLAIMS*Suba*

1. The use of:
- (i) EtxB, CtxB or VtxB free from whole toxin;
- (ii) an agent other than EtxB or CtxB, having GM1-binding activity, or an agent other than VtxB having Gb3-binding activity; or
- (iii) an agent having an effect on intracellular signalling events mediated by GM1-binding or Gb3 binding;
- as an immunomodulator for a vaccine against infectious diseases.
2. ^{A method} ~~The use~~ according to claim 1, wherein the immunomodulator is EtxB free from whole toxin.
3. ^{A method} ~~The use~~ according to claim 1 or 2, wherein the infectious disease is one for which the infectious agent is a member of the herpes virus family.
4. ^{A method} ~~The use~~ according to claim 3, wherein the infectious disease is caused by an infectious agent, and the infectious agent is selected from the group consisting of HSV-1, HSV-2, EBV, VZV, CMV, HHV-6, HHV-7 and HHV-8.
5. ^{A method} ~~The use~~ according to claim 4, wherein the infectious agent is selected from the group consisting of HSV-1, HSV-2, CMV or EBV.
6. ^{A method} ~~The use~~ according to claim 1 or 2, wherein the infectious disease is caused by an infectious agent, and the infectious agent is an influenza virus.
7. ^{A method} ~~The use~~ according to claim 1 or 2, wherein the infectious disease is caused by an infectious agent, and the infectious agent is a parainfluenza virus.
8. ^{A method} ~~The use~~ according to claim 1 or 2, wherein the infectious disease is caused by an infectious agent, and the infectious agent is a respiratory syncytial virus.
9. ^{A method} ~~The use~~ according to claim 1 or 2, wherein

the infectious disease is caused by an infectious agent, and the infectious agent is a hepatitis virus.

10. ^{A method} ~~The use~~ according to claim 9, wherein the infectious agent is selected from the group consisting of hepatitis A, B, C and D viruses.

11. ^{A method} ~~The use~~ according to claim 10, wherein the infectious agent is a hepatitis A virus or a hepatitis C virus.

12. ^{A method} ~~The use~~ according to claim 1 or 2, wherein the infectious disease is meningitis.

13. ^{A method} ~~The use~~ according to claim 12, wherein the infectious disease is caused by an infectious agent, and the infectious agent is selected from the group consisting of *Neisseria meningitidis*, *Haemophilus influenzae* type B and *Streptococcus pneumoniae*.

14. ^{A method} ~~The use~~ according to claim 1 or 2, wherein the infectious disease is pneumonia or a respiratory tract infection.

15. ^{A method} ~~The use~~ according to claim 14, wherein the infectious disease is caused by an infectious agent, and the infectious agent is selected from the group consisting of *Streptococcus pneumoniae*, *Legionella pneumophila* and *Mycobacterium tuberculosis*.

16. ^{A method} ~~The use~~ according to claim 1 or 2, wherein the infectious disease is a sexually-transmitted disease.

17. ^{A method} ~~The use~~ according to claim 16, wherein the infectious disease is caused by an infectious agent, and the infectious agent is selected from the group consisting of *Neisseria gonorrhoeae*, HIV-1, HIV-2 and *Chlamydia trachomatis*.

18. ^{A method} ~~The use~~ according to claim 1 or 2, wherein the infectious disease is a gastrointestinal disease.

19. ^{A method} ~~The use~~ according to claim 18, wherein the infectious disease is caused by an infectious agent,

and the infectious agent is selected from the group consisting of enteropathogenic, enterotoxigenic, enteroinvasive, enterohaemorrhagic and enteroaggregative *E.coli*, rotavirus, *Salmonella enteritidis*, *Salmonella typhi*, *Helicobacter pylori*, *Bacillus cereus*, *Campylobacter jejuni* and *Vibrio cholerae*.

20. ^{A method} The use according to claim 1 or 2, wherein the infectious disease is a superficial infection.

21. ^{A method} The use according to claim 20, wherein the infectious disease is caused by an infectious agent, and the infectious agent is selected from the group consisting of *Staphylococcus aureus*, *Streptococcus pyogenes* and *Streptococcus mutans*.

22. ^{A method} The use according to claim 1 or 2, wherein the infectious disease is a parasitic disease.

23. ^{A method} The use according to claim 22, wherein the infectious disease is caused by an infectious agent, and the infectious agent is selected from the group consisting of malaria, *Trypanasoma* spp., *Toxoplasma gondii*, *Leishmania donovani* and *Oncocerca* spp.

24. A vaccine composition for use against an infectious disease, which infectious disease is caused by an infectious agent, wherein the vaccine composition comprises an antigenic determinant and an immunomodulator selected from:

- (i) EtxB, CtxB or VtxB free from whole toxin;
- (ii) an agent other than EtxB or CtxB, having GM1-binding activity, or an agent other than VtxB having Gb3-binding activity; or
- (iii) an agent having an effect on intracellular signalling events mediated by GM1-binding or Gb3 binding;

wherein said antigenic determinant is an antigenic

007627 24/04/2000

determinant of said infectious agent.

25. A vaccine composition according to claim 24 in which the infectious disease is HSV-1 infection and wherein the antigenic determinant is an antigenic determinant of HSV-1.

26. A vaccine composition according to claim 24 or 25 in which the immunomodulator is EtxB free from whole toxin.

27. A vaccine composition according to claim 24, 25 or 26 in which the immunomodulator and the antigenic determinant are separate moieties.

28. A vaccine composition according to claim 24, 25 or 26 in which the immunomodulator and the antigenic determinant are linked by a bifunctional crosslinking reagent.

29. A kit for vaccination of a mammalian subject against an infectious disease, which kit comprises:

a) one of the following agents:

(i) EtxB, CtxB or VtxB free from whole toxin;

(ii) an agent other than EtxB or CtxB, having GM1-binding activity, or an agent other than VtxB having Gb3-binding activity; or

(iii) an agent having an effect on intracellular signalling events mediated by GM1-binding or Gb3 binding; and

b) an antigenic determinant which is an antigenic determinant of the infectious disease, for coadministration with the said vaccine immunomodulator.

30. A method of preventing or treating a disease in a host, which method comprises the step of inoculating said host with a vaccine comprising at least one antigenic determinant and an immunomodulator, where the immunomodulator is:

(i) EtxB, CtxB or VtxB free from whole toxin;

(ii) an agent other than EtxB or CtxB, having GM1-binding activity, or an agent other than VtxB having

Gb3-binding activity; or

(iii) an agent having an effect on intracellular signalling events mediated by GM1-binding or Gb3 binding.

5 ~~2~~ §1. The use of:

5
Sub A2

(i) EtxB, CtxB or VtxB free from whole toxin;

(ii) ~~an agent other than EtxB or CtxB, having GM1-binding activity, or an agent other than VtxB having Gb3-binding activity; or~~

10 (iii) an agent having an effect on
intracellular signalling events mediated by GM1-binding
or Gb3 binding

to upregulate the production of antibodies at mucosal surfaces.

15 32. The use of:

(i) EtxB, CtxB or VtxB free from whole toxin;

(ii) an agent other than EtxB or CtxB, having GM1-binding activity, or an agent other than VtxB having Gb3-binding activity; or

20 (iii) an agent having an effect on
intracellular signalling events mediated by GM1-binding
or Gb3 binding;

as an immunomodulator in a vaccine, to prolong antigen presentation and give sustained immunological memory in a mammalian subject.

33. A vaccine composition for use against an infectious disease, which infectious disease is caused by an infectious agent, which vaccine comprises an antigenic determinant and a immunomodulator selected from: ^{the group consisting of}

(i) EtxB, CtxB or VtxB free from whole toxin;

(ii) an agent other than EtxB or CtxB, having GM1-binding activity, or an agent other than VtxB having Gb3-binding activity; ^{and} ~~or~~

35 (iii) an agent having an effect on
intracellular signalling events mediated by GM1-binding

wherein said antigenic determinant is an antigenic determinant of said infectious agent and wherein the immunomodulator prolongs presentation of the antigenic determinant and gives sustained immunological memory.

(i) EtxB, CtxB or VtxB free from whole toxin;
(ii) an agent other than EtxB or CtxB, having GM1-binding activity, or an agent other than VtxB having Gb3-binding activity; or
(iii) an agent which has an effect on vesicular internalisation mediated by GM1-binding or Gb3 binding;

35. The use of:

in a conjugate with antigen or antigenic determinant to upregulate the presentation of said antigenic determinant, or an antigenic determinant derived from said antigen, by MHC class I molecules.

- a) EtxB, CtxB, or an agent other than EtxB or CtxB which has GM1-binding activity; and
- b) an EBV antigen

37. A therapeutic composition which comprises:

- 46 -

EtxB, CtxB or an agent other than EtxB or CtxB
which has GM1-binding activity
for use in the treatment of EBV-associated
diseases.

5

[illegible]